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Intravenous prostaglandin F2α and amniotomy for the elective induction of labor at term

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In an earlier trial [7, 11] with intravenously administered PGF2α for the elective induction of multiparae at term, amniotomy was delayed to comply with FDA regulations. As a consequence, the start of the electronic supervision was also postponed and thus the refined assessment of the potential fetal hazards of PGF2α was prevented.
The present study was tailored in accordance with the dual purpose of meeting our primary objective (to study the effects of PGF2α in the fetus and the newborn) by relying on a procedure actually used in clinical obstetrics, i. e. amniotomy followed by the intravenous infusion of an oxytocic drug.

1. Materials and methods

Since we wished to study the fetal effects of PGF2α in association with amniotomy, any other factor that might influence the unborn had to be eliminated. This explains the selection criteria, which have been discussed elsewhere [6]. Because inductions were performed on a elective basis, the candidates had to be inducible according to the BISHOP pelvic scoring system [1].
The standardized protocol was as follows. The 73 candidates admitted to hospital were examined and evaluated as to inducibility by the same obstetrician (M.T.). **Low amniotomy was then performed** and **fetal monitoring immediately started.** Uterine activity was recorded by means of an **open-tip catheter inserted transcervically,** and the instaneous heart rate (FHR) was calculated from the **scalp electrode fetal signal** [8]. If, after 60 minutes of observation, the patient was judged to be in active labor, no oxytocic drugs were administered and she was excluded from the study. Among those excluded were 18 women (8 primi- and 10 multiparae) in whom the intra-amniotic pressure variations occurring within 60 minutes after artificial rupture of the membranes were indicative of active labor (> 100 Montevideo Units).
This left us with a **total of 55 women** (30 primi- and 25 multiparae) **induced by amniotomy and PGF2α.** One hour after membrane rupture the intravenous infusion, by pump, of PGF2α in normal saline was started. The dose level was titrated against the uterine response; starting

Curriculum vitae

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at 2.0 μg/min, **the dose was increased at intervals of 15—60 minutes until "adequate" contractions were recorded.** From then on and usually up to the time of delivery, this dose level was maintained. However, if signs indicating uterine hyperstimulation (tachysystolia, hypertonus) were obtained or pathologic FHR patterns recorded (Tab. IV and V), the dosage was decreased and in occasional cases the infusion was stopped; in some of these cases the infusion was carefully resumed after the recordings had returned to normal.

The criteria of normal **first stage** myometrial activity and FHR patterns have been described previously [10]. During the **second stage** of labor a number of FHR patterns can be recorded that are associated with a typical fetal ouctome [9]. Knowledge of these patterns is of paramount importance for the interpretation of the biochemical and clinical state of the infant at birth, this state usually reflecting the events that have taken place during the second stage of labor. Because knowledge of the biochemical status of the fetus at the end of the first stage is indispensible for the evaluation of the fetal drug response during this period, **we systematically assessed the scalp blood pH at full dilation** according to SALING's method [4].

Second-stage uterine activity is considered abnormal (prolonged expulsion) when more than 10 forceful (> 110 mmHg) expulsive contractions are recorded. In one patient (A 11) the

Tab. II. Relevant details concerning the induction in primiparae (n = 30).

Case no.	Age [yrs]	G. A.	B. S.	Interval* (h:min) from start of PG infusion to: A	B	M. D. L. [μg/min]	T. D. [mg]	M. D.	M. S. E.
A 01	29	39	9	4:36	5:03	40	5.0	S	0
A 02	24	39	9	2:28	3:13	40	2.5	VE	0
A 03	26	39	8	5:48	6:06	10	5.4	S	0
A 04	28	39	7	5:50	6:45	10	1.8	VE	0
A 05	24	38	8	2:08	3:00	4	0.4	S	0
A 06	20	40	5	5:33	5:41	10	2.7	S	0
A 07	25	40	5	5:03	5:08	20	4.9	S	0
A 08	22	40	8	2:26	2:36	20	2.8	S	0
A 09	19	39	6	6:14	6:31	10	3.9	S	0
A 10	18	39	9	4:12	4:46	20	4.3	S	0
A 11	23	39	10	2:45	3:05	20	2.0	S	0
A 12	19	38	6	5:32	5:52	2	3.6	S	0
A 13	24	39	6	12:02	12:20	10	7.5	S	0
A 14	23	39	6	6:18	6:40	10	3.9	S	0
A 15	18	38	7	5:26	5:48	2	0.8	S	0
A 16	24	38	6	10:20	10:35	4	3.1	VE	0
A 17	26	39	7	3:16	4:38*	20	3.5	S	0
A 18	21	40	5	13:17	13:35	20	6.5	S	0
A 19	26	39	6	7:23	7:33	10	4.7	VE	0
A 20	25	38	6	7:49	7:59*	20	4.8	VE	vomiting
A 21	20	40	5	13:06	13:12	10	8.0	S	0
A 22	24	39	7	3:27	3:42	10	2.5	VE	0
A 23	26	39	4	6:30	6:45	20	6.7	S	0
A 24	21	39	7	6:41	6:46	20	3.5	S	0
A 25	23	40	4	6:19	6:30	10	4.6	S	0
A 26	16	39	6	5:29	5:49	20	4.7	VE	0
A 27	25	39	4	15:44	15:59	40	16.1	VE	0
A 28	25	38	6	5:02	5:17*	40	3.5	VE	vomiting
A 29	30	40	7	4:37	4:49	20	4.5	VE	0
A 30	29	39	6	7:35	8:00	10	5.2	VE	0

* For symbols and abbreviations see Tab. II.

uterine contractions could not be recorded because attachment of the intra-uterine catheter failed. A technical defect also prevented us from recording the FHR during the second stage of labor in three other cases (A 10, B 13 and B 19).

Progress of labor was assessed on the basis of cervical dilatation and effacement. **Delivery was spontaneous (n = 41)** or assisted by **vacuum extraction (n = 14).** At birth, the biochemical and clinical (1- and 5-minute APGAR scores) **states of the infant were assessed.** For the former, blood samples obtained from the umbilical artery and vein and from the maternal femoral artery were tested for parameters related to the acid-base and lactate-pyruvate equilibria [2, 5, 6].

2. Results

2.1 Efficacy

The induction was successful in all of the cases (Tab. I and II). The duration of the infusion ranged from 2 hours and 36 minutes to 15 hours and 59 minutes in primiparae (mean: 6:47 ± 0:36 h:min) and from 2 hours and 30 minutes to 16 hours and 48 minutes in multiparous women (mean: 4.49 ± 0.55 h:min). **The total dose** of PGF2α necessary to accomplish the delivery also **varied widely:** from 0.4 to 16.1 mg (mean: 4.4 ± 0.5 mg) in primiparae and from 0.6 to 25.6 mg (mean: 4.1 ± 0.9 mg) in multiparae.

Tab. II. Relevant details concerning the induction in multiparae (n = 25).

Case no.	Age [yrs]	P.	G. A. [weeks]	B. S.	Interval (h:min) from start of PG infusion to: A	B	M. D. L. [μg/min]	T. D. [mg]	M. D.	M. S. E.
B 01	28	2	38	4	4:23	4:25	20	4.0	S	0
B 02	21	1	38	6	4:13	4:19	4	1.9	VE	0
B 03	21	1	39	8	4:50	5:00	4	2.1	S	0
B 04	26	1	38	8	3:00	3:10	40	3.1	S	0
B 05	24	1	39	5	6:53	6:58	40	9.4	S	0
B 06	23	1	38	5	5:31	5:42	4	1.6	S	0
B 07	21	1	39	7	3:12	3:25	20	2.4	S	0
B 08	24	5	41	9	3:12	3:44	10	1.8	S	0
B 09	27	1	39	6	5:08	5:13	20	5.9	S	0
B 10	27	1	39	4	4:53	5:00	20	5.6	S	0
B 11	33	1	39	7	4:16	4:25	20	3.9	VE	0
B 12	27	1	39	8	2:36	2:41	10	1.4	S	0
B 13	24	1	38	4	6:16	6:32	20	7.0	S	0
B 14	27	1	38	6	4:42	4:46	20	3.6	S	0
B 15	29	4	40	6	2:55	3:09	40	5.2	S	0
B 16	28	1	38	5	5:29	5:39	10	1.3	S	0
B 17	31	3	40	5	4:51	4:54	10	3.6	S	0
B 18	23	1	40	7	3:02	3:05	10	1.9	S	0
B 19	26	1	39	6	4:12	4:18	10	2.2	S	0
B 20	40	1	39	9	3:11	3:18	4	0.6	VE	0
B 21	25	1	41	6	16:39	16:48	100	25.6	S	0
B 22	38	1	40	6	4:30	4:38	20	4.2	S	0
B 23	27	1	38	9	2:31	2:38	10	1.4	S	0
B 24	26	1	38	7	3:54	4:00	10	2.1	S	0
B 25	28	1	39	7	2:15	2:30	20	1.7	S	0

* Since as a rule, the PG infusion was administered continuously until the delivery proper, the time values indicated correspond with the duration of the infusion. Exceptions are indicated with an asterisk.

P. = parity; G. A. = gestational age [weeks]; B. S. = BISHOP score; A = full dilatation; B = delivery; M. D. L. = maximal dose level [μg/min]; T. D. = total dose [mg]; M. D. = mode of delivery: S = spontaneous, VE = by vacuum extraction; M. S. E. = maternal side effects.

Tab. III. Maternal biochemical status at delivery (A. femoralis).

		L/P	pH	BE [mEq/l]	SB [mEq/l]	PCO_2 [mmHg]	PO_2 [mmHg]
Primiparae	PGF2α	12.79±1.07 (29)	7.389±0.009 (30)	—8.62±0.50 (30)	17.71±0.35 (30)	26.0±1.0 (29)	99.0±1.9 (28)
	Controls	12.55±0.49 (56)	7.374 0.004 (47)	—8.41±0.33 (47)	17.70±0.24 (47)	27.6±1.7 (15)	100.0±1.5 (40)
	t-test (Student)	0.23	1.62	0.36	0.02	0.88	0.40
Multiparae	PGF2α	12.68±0.46 (25)	7.388±0.004 (24)	—6.42±0.51 (24)	19.26±0.37 (24)	28.5±0.9 (24)	96.5±2.2 (24)
	Controls	13.05±0.32 (104)	7.394±0.005 (81)	—6.81±0.24 (80)	18.82±0.17 (80)	29.1±0.9 (32)	96.3±1.2 (73)
	t-test (Student)	0.54	0.46	0.76	1.17	0.49	0.06

* Mean values ± SE. The number of cases is given in brackets. L and P = lactate and pyruvate. BE and SB = base excess and standard bicarbonate.

Tab. IV. Monitoring, biochemical and clinical data (primiparae).

Case no.	First stage of labor	pH_s	Second stage of labor	Apgar*	pH_a
A 01	Transient hypertonus + type-III dips	7.42	0	7—9	7.24
A 02	0	7.25	0	9—9	7.25
A 03	0	7.29	0	9—9	7.30
A 04	0	7.36	Prolonged expulsion	8—8	7.27
A 05	0	7.45	Prolonged expulsion	6—9	7.24
A 06	0	7.46	0	9—9	7.40
A 07	0	7.31	0	5—7	7.21
A 08	0	7.35	0	9—9	7.34
A 09	0	7.39	0	9—9	7.25
A 10	0	7.39	No recording (technical defect)	9—9	7.24
A 11	No tocogram; tachygram normal	7.31	No tocogram; tachygram normal	8—9	7.26
A 12	0	7.44	0	8—9	7.27
A 13	0	7.29	0	9—9	7.29
A 14	0	7.34	0	4—9	7.42
A 15	0	7.36	0	9—9	7.26
A 16	0	7.37	0	7—9	7.37
A 17	0	7.40	Transient bradycardia	8—9	7.33
A 18	0	7.29	Prolonged expulsion	8—9	7.28
A 19	0	7.30	0	8—9	7.31
A 20	Transient hypertonus, brady.	6.92	0	7—9	6.98
A 21	0	7.40	0	9—9	7.35
A 22	Variable decelerations	7.26	0	8—8	7.21
A 23	0	7.30	0	6—9	7.24
A 24	0	7.41	0	9—9	7.38
A 25	0	7.42	0	9—9	7.26
A 26	0	7.23	Transient bradycardia	7—9	7.30
A 27	0	7.25	Progressive bradycardia	2—8	7.13
A 28	Vomit., transient hypertonus	7.31	0	8—9	7.26
A 29	0	7.28	0	7—9	7.23
A 30	0	7.27	0	7—9	7.18

* For symbols and abbreviations see Tab. V.

2.2 Maternal morbidity

Maternal side-effects were not a problem. **Vomiting** was observed in 2 primiparae (B 20 and B 28). In one of these (A 20) it is not even clear whether the vomiting should be ascribed to PGF2α or to ritodrine. It is noteworthy that one patient (B 21) who received a very high dose of PFG2α (infusion rate up to 100 μg/min; total dose 25.6 mg) did not show any disturbing effects.

The mean arterial acid-base values in the mother at the time of delivery (Tab. III) showed no statistically significant deviations from the norm [3].

2.3 Monitoring data

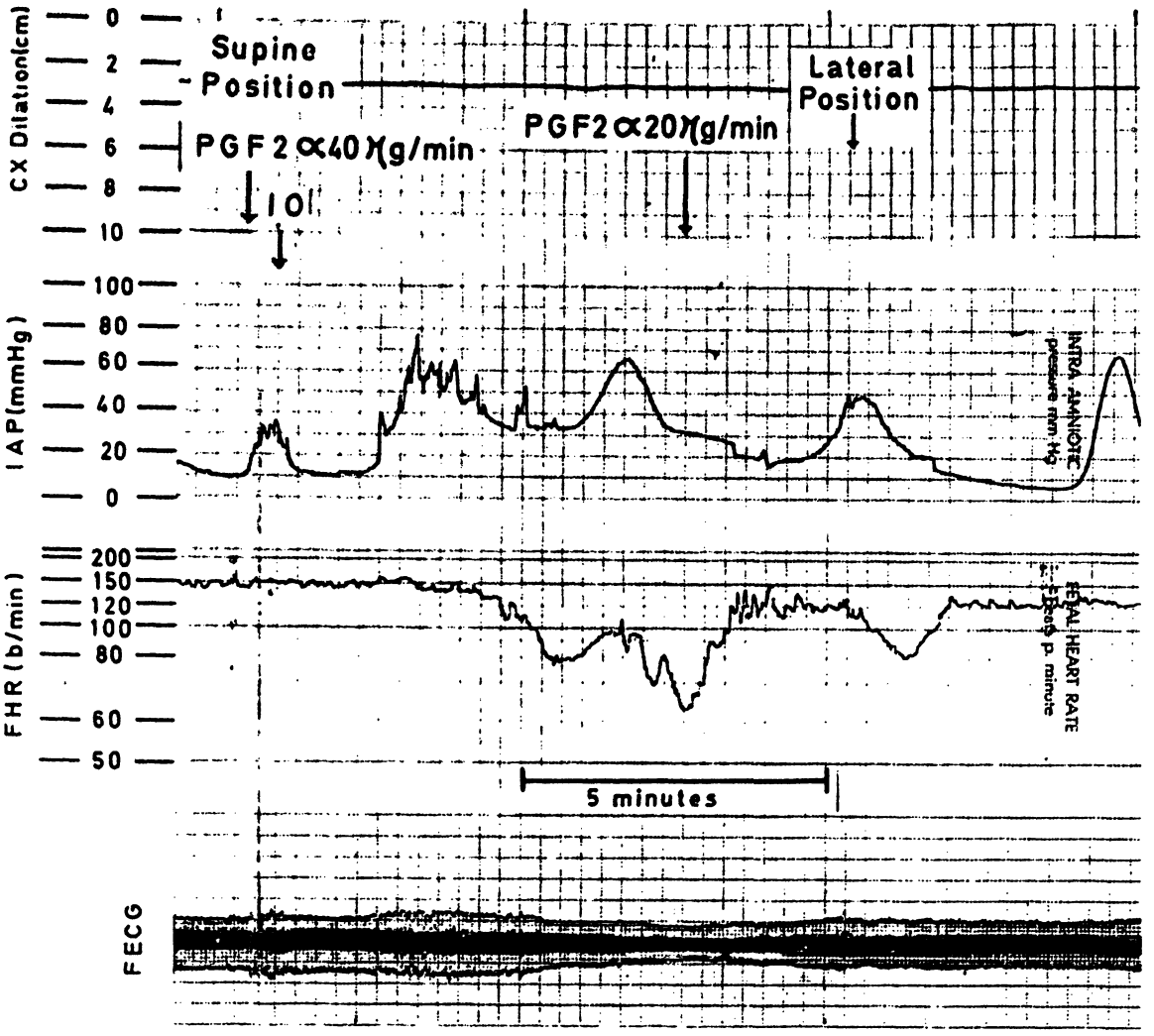
Monitoring data as well as the essential clinical and biochemical data are listed in Tab. IV and V. Some abnormalities are illustrated in Figs. 1—7.

In the multiparae the tocotachygrams were normal. **In three primiparae** (A 01, A 20 and A 28) **first-stage labor was complicated by transient hypertonus.** Two of these (A 01 and A 20) showed simultaneous FHR anomalies (Figs. 1—4). Only one fetus (A 20) was found to be acidotic and hypoxic at the time of birth. Another abnormal first-stage finding was **bouts of variable deceleration** in one case (A 22, Fig. 5), but without any pre- or postnatal influence on the child. The following second-stage abnormalities were recorded: **prolonged expulsion** (3 instances) without untoward fetal effects, **transient bradycardia** (A 17 and A 26, Fig. 6) and **progressive bradycardia** (A 27, Fig. 7).

Tab. V. Monitoring, biochemical and clinical data (multiparae).

Case no.	First stage of labor	pH_s	Second stage of labor	Apgar*	pH_a
B 01	0	7.33	0	9—9	7.35
B 02	0	7.33	0	5—7	7.36
B 03	0	7.40	0	8—9	7.39
B 04	0	7.36	0	8—9	7.35
B 05	0	7.32	0	9—9	7.35
B 06	0	7.41	0	9—9	7.28
B 07	0	7.33	0	9—10	7.32
B 08	0	7.33	0	9—10	7.33
B 09	0	7.34	0	9—9	7.37
B 10	0	7.34	0	9—9	7.35
B 11	0	7.39	0	8—9	7.25
B 12	0	7.33	0	7—9	7.30
B 13	0	7.39	No recording (technical defect)	9—9	7.27
B 14	0	7.31	0	7—8	7.28
B 15	0	7.26	0	6—6	7.23
B 16	0	7.33	0	7—8	7.39
B 17	0	7.36	0	7—8	7.38
B 18	0	7.41	0	9—9	7.36
B 19	0	7.39	No recording (technical defect)	9—9	7.31
B 20	0	7.35	0	8—9	7.30
B 21	0	7.20	0	9—10	7.16
B 22	0	7.35	0	9—9	7.34
B 23	0	7.33	0	8—9	7.25
B 24	0	7.32	0	4—9	7.30
B 25	0	7.27	0	5—9	7.24

Key to symbols: 0 = no abnormalities
pH_s = actual pH in scalp blood
pH_a = actual pH measured in blood of umbilical artery
* 1- and 5-minute Apgar scores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0
2
4
6
8
10
Supine Position
PGF2∝40γg/min
10'
PGF2∝20γg/min
Lateral Position
IAP(mmHg)
100
80
60
40
20
0
INTRA AMNIOTIC pressure mm Hg
FHR (b/min)
200
150
120
100
80
60
50
FETAL HEART RATE beats p. minute
5 minutes
FECG

Fig. 1

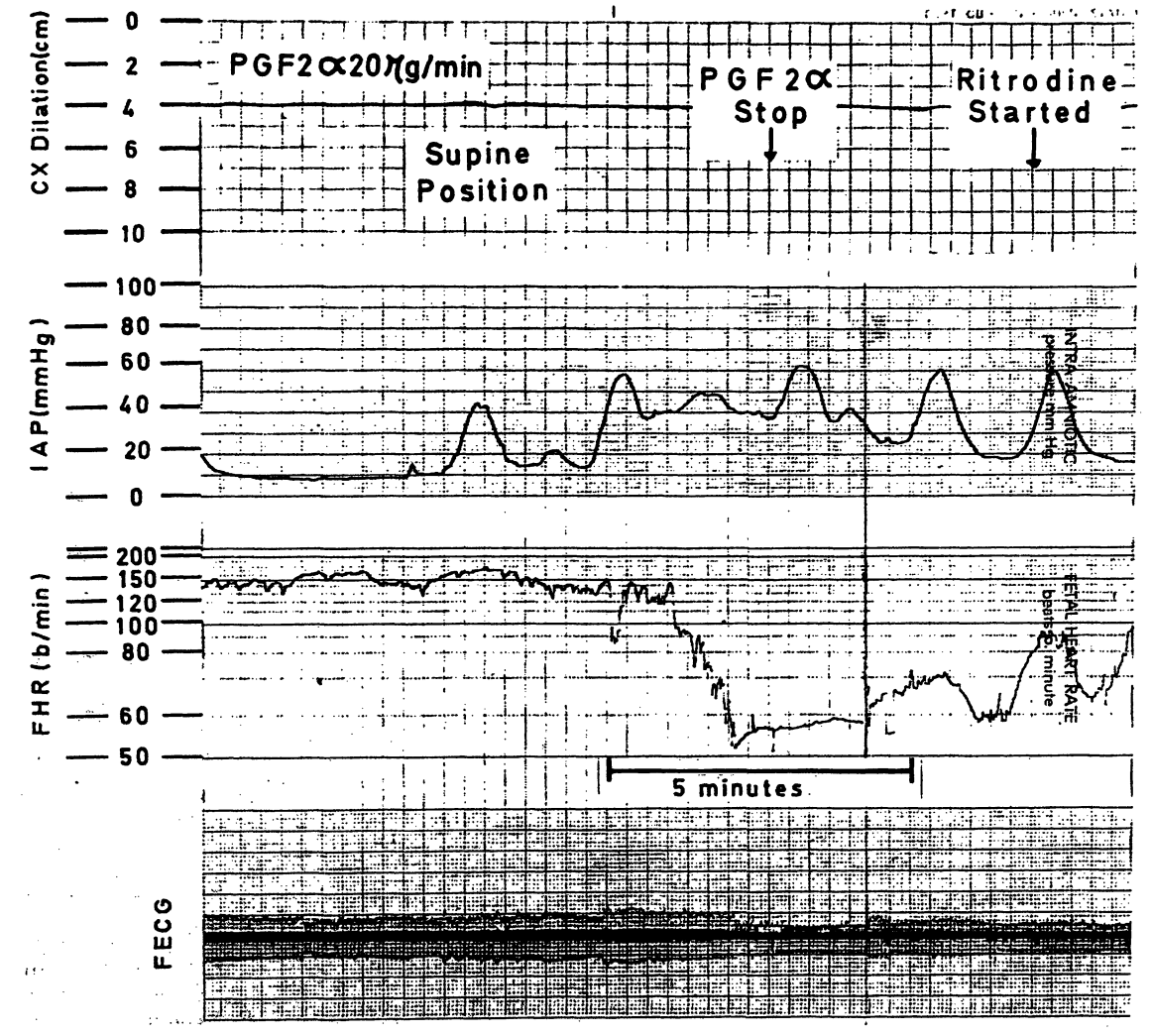
CX Dilation(cm)
0
2
4
6
8
10
PGF2∝20γg/min
PGF2∝ Stop
Ritrodine Started
Supine Position
IAP(mmHg)
100
80
60
40
20
0
INTRA AMNIOTIC pressure mm Hg
FHR (b/min)
200
150
120
100
80
60
50
FETAL HEART RATE beats p. minute
5 minutes
FECG

Fig. 2

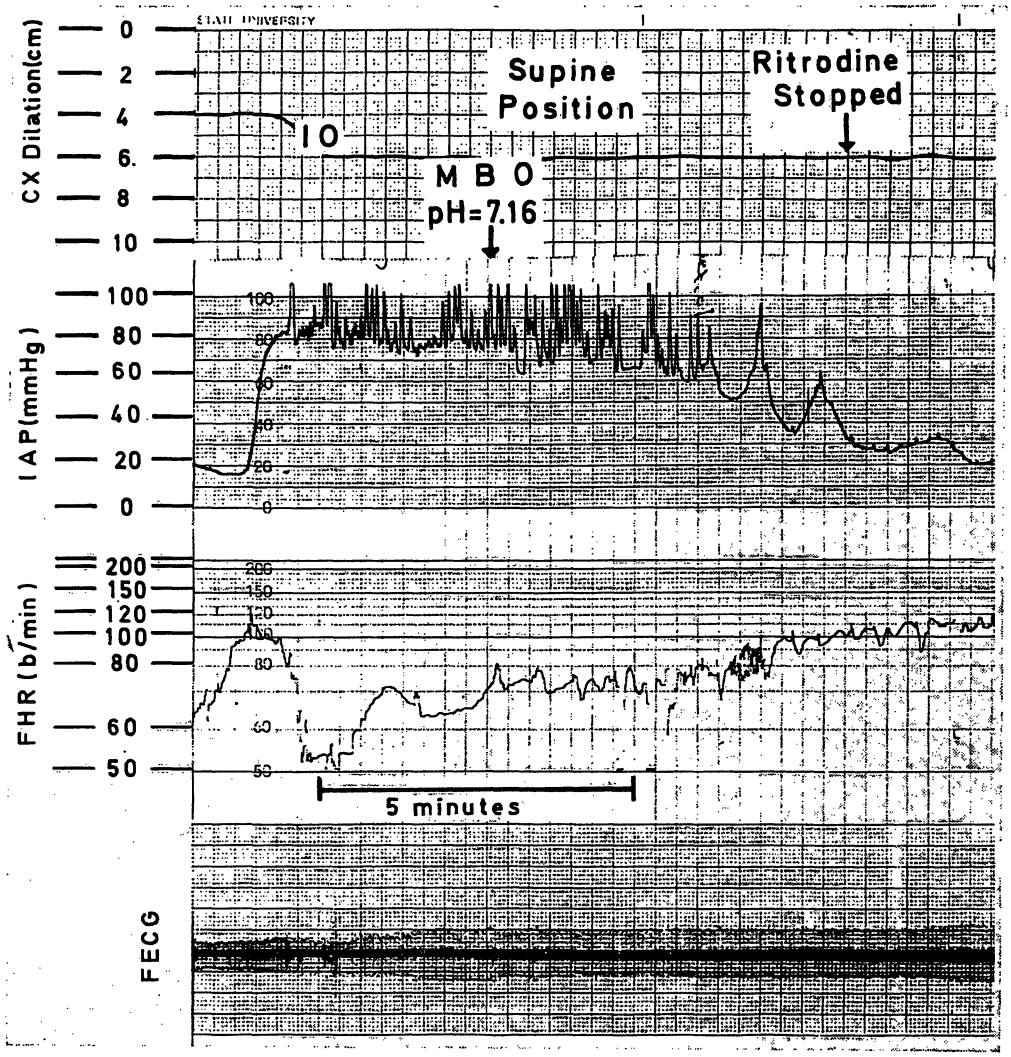

Fig. 3

Fig. 1. Case A 01. The dosage level of intravenous PGF2α was increased from 20 to 40 μg/min. Pelvic examination (IO) showed the cervical dilatatation to be 3 cm. Movements of the patient and an attempt at passing urine were associated with a bout of late FHR deceleration lasting for 7 min. The infusion was decreased to the previous dosage level and the patient turned on her side. pH_s = 7.42. Second stage of labor normal. Infant normal at birth (APGAR scores 7—9; pH = 7.24).

Fig. 2. Case A 20. Cervical dilatation 4 cm. Slack uterine contractions despite the intravenous infusion of 20 μg/min PGF2α for more than one hour. Without any warning, uterine hypertonus occurred accompanied by intense fetal bradycardia. The PG infusion was immediately stopped. This was followed by the decrease of the intra-amniotic pressure and the recovery of the FHR. An intravenous drip of a high dose of Ritodrine (5 mg/min) was started (continued on Fig. 3).

Fig. 3. Case A 20. The infusion of Ritodrine (see Fig. 2) was followed by intense vomiting lasting for seven minutes and associated with severe fetal bradycardia. At this time, the scalp blood pH (MBO) was 7.16. Vomiting diminished and the basal tonus together with the FHR tended to return to normal. The infusion of Ritodrine was stopped (continued on Fig. 4).

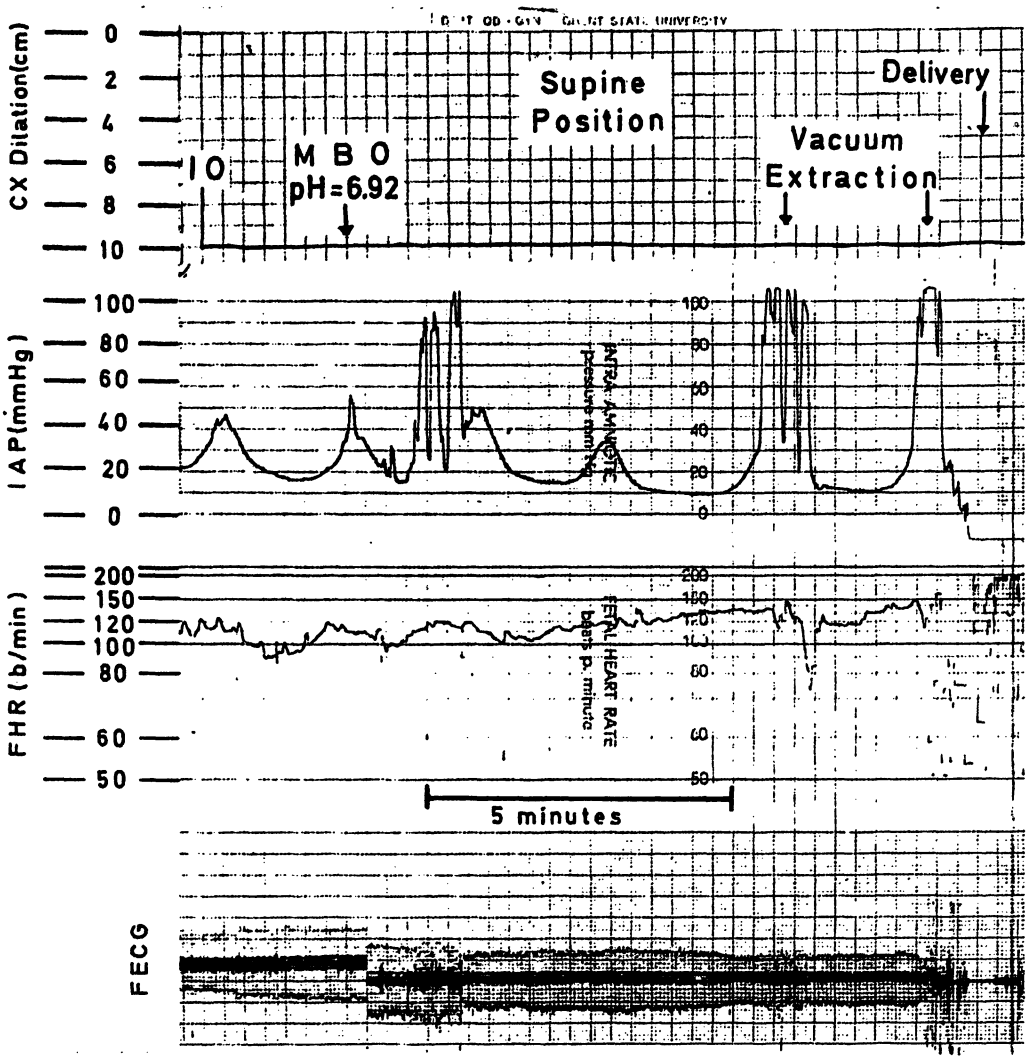
CX Dilation(cm)
0
2
4
6
8
10
IO
M B O
pH=6.92
Supine
Position
Delivery
Vacuum
Extraction
IAP(mmHg)
100
80
60
40
20
0
FHR (b/min)
200
150
120
100
80
60
50
5 minutes
FECG

Fig. 4

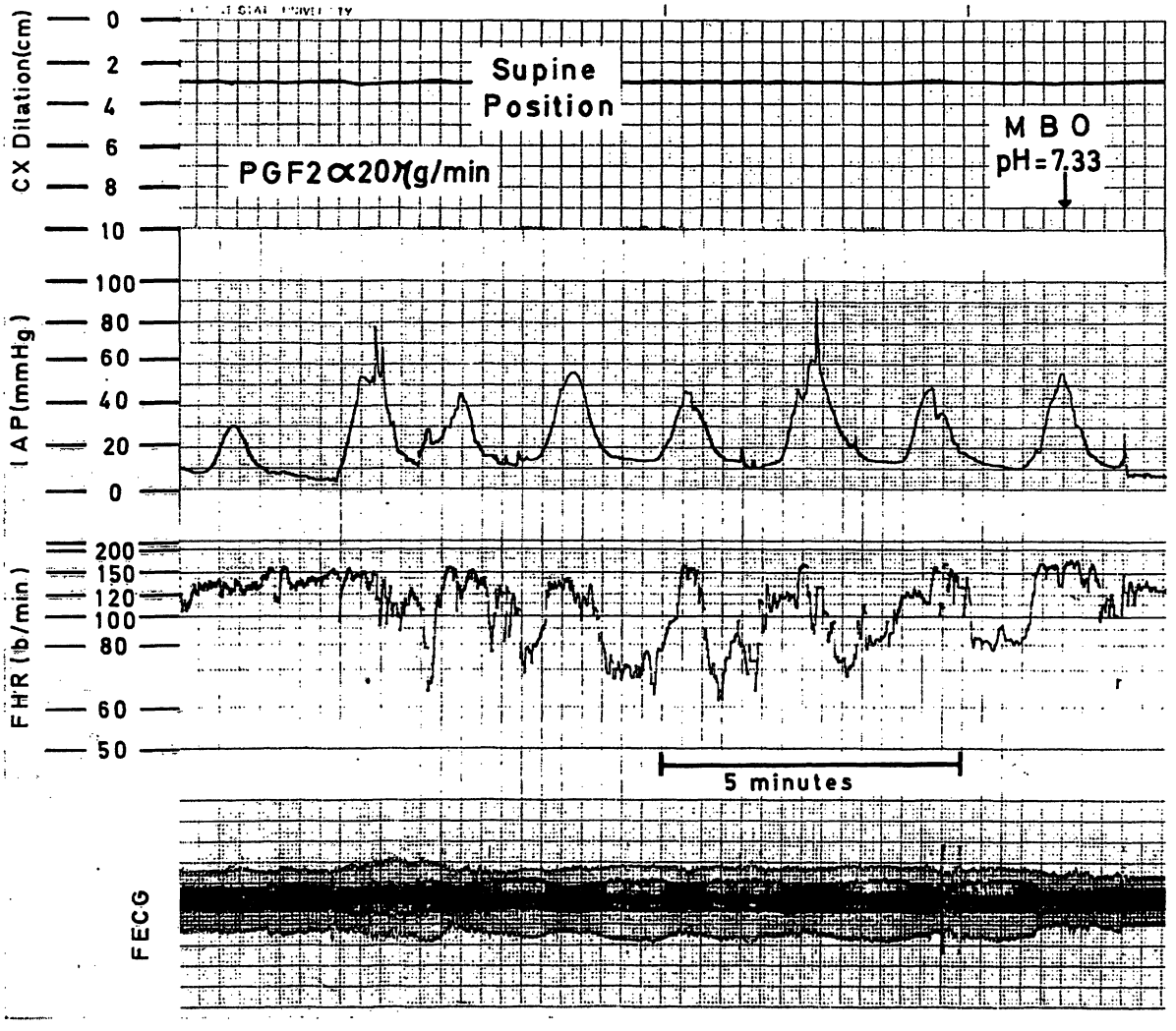
CX Dilation(cm)
0
2
4
6
8
10
Supine
Position
PGF2∝20γg/min
M B O
pH=7.33
IAP(mmHg)
100
80
60
40
20
0
FHR (b/min)
200
150
120
100
80
60
50
5 minutes
FECG

Fig. 5

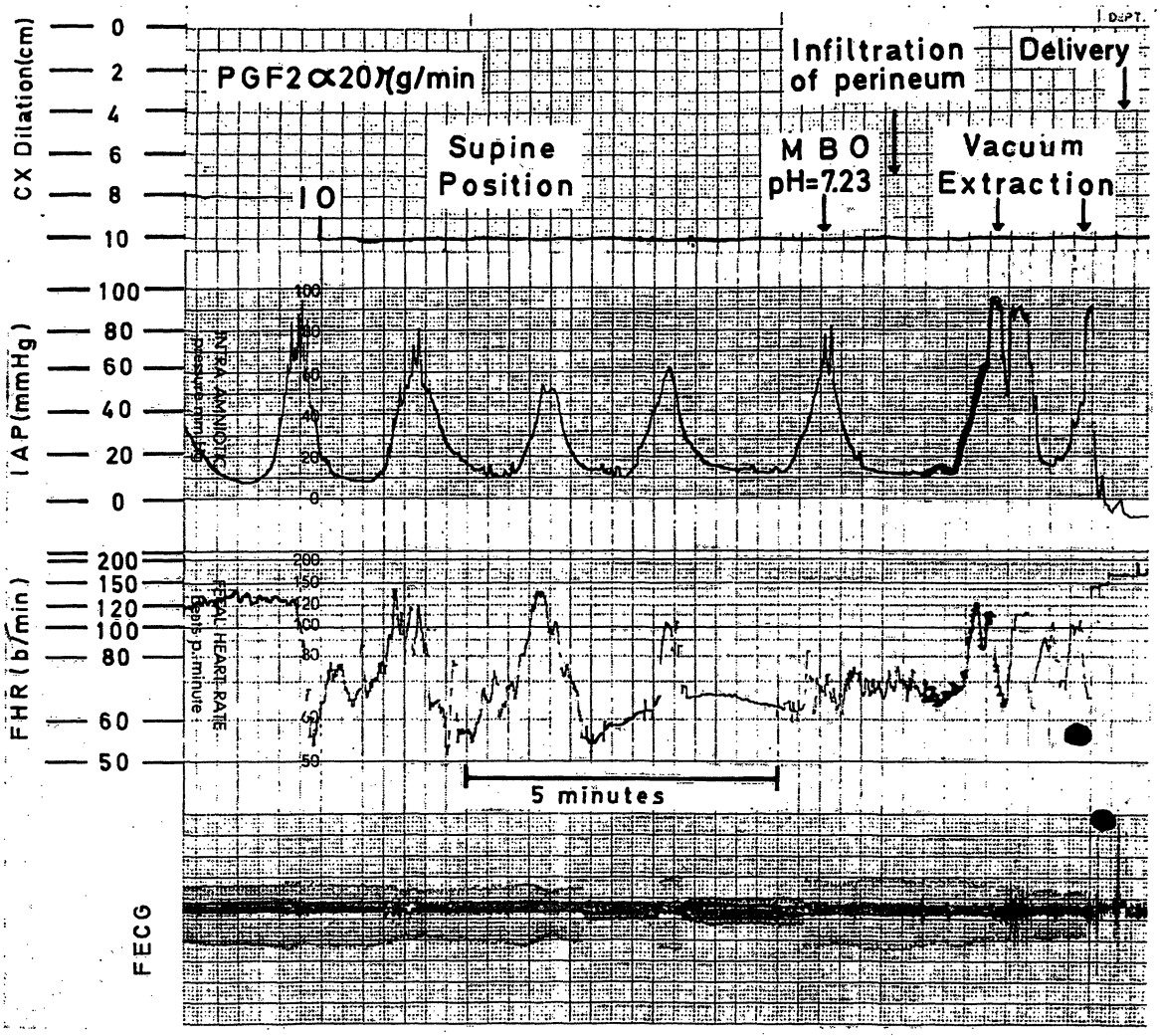

Fig. 6

Fig. 4. Case A 20. Vaginal examination (IO) showed the cervix to be fully dilated (see also Fig. 3) and the scalp blood pH (MBO) was 6.92. The delivery was readily accomplished by two tractions with the vacuum extractor. At birth, the infant appeared to be clinically normal (APGAR-scores 7—9; $pH_a = 6.98$).

Fig. 5. Case A 22. Appearance of (mild) variable deceleration of the FHR in the supine position which disappeared on turning the patient on her left side. Scalp blood pH = 7.33 (MBO). At birth, the child was normal (APGAR scores 8—8; $pH_a = 7.21$).

Fig. 6. Case A 26. After an uneventful first stage of labor, expulsive contractions were accompanied by FHR deceleration (variable deceleration type) with one instance of lack of return to the baseline FHR (transient bradycardia). The delivery was achieved by vacuum extraction which was readily carried out. At birth, the cord was found to be wrapped around the baby's neck. The infant was normal (APGAR scores 7—8; $pH_a = 7.30$).

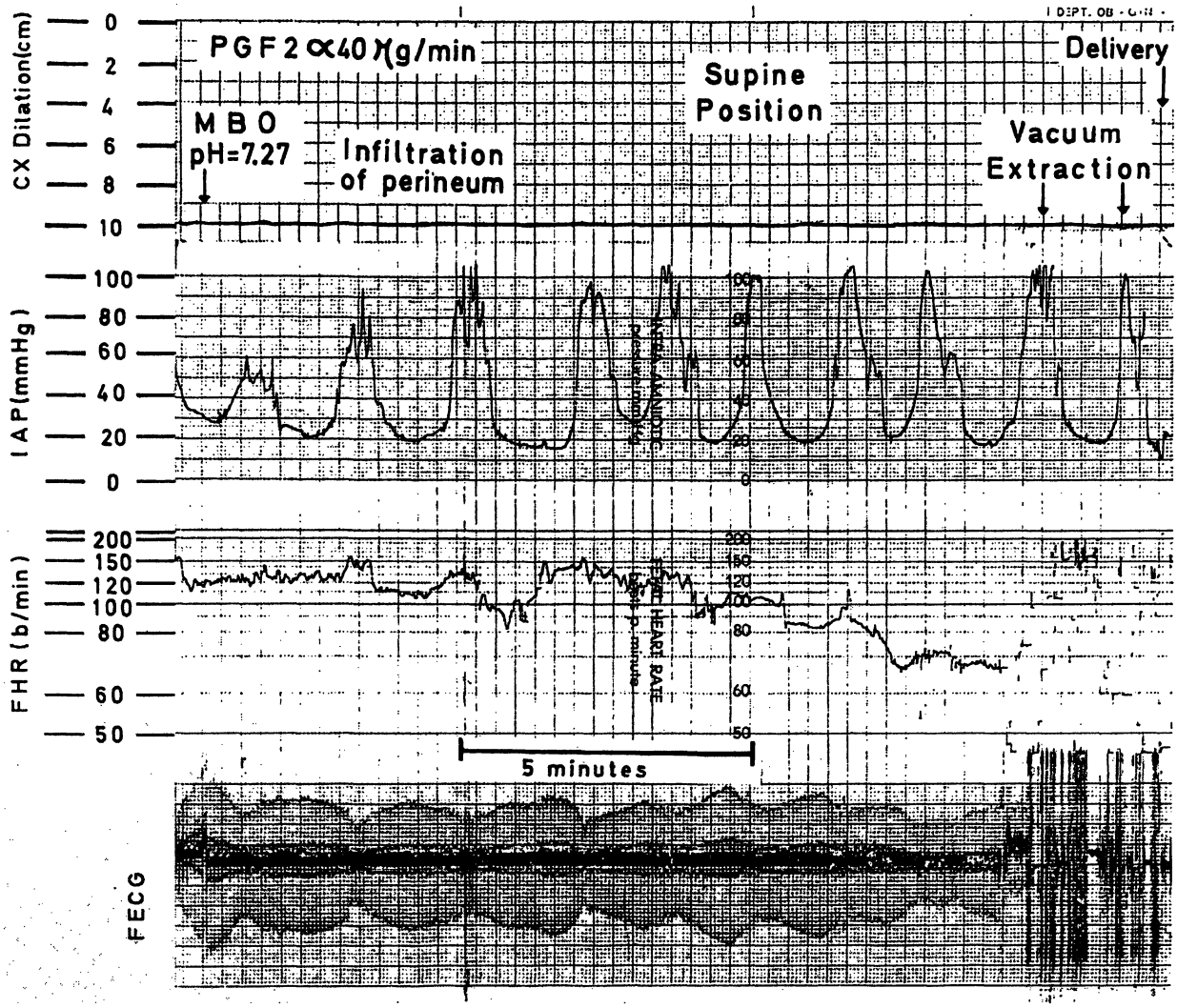

Fig. 7. Case A 27. At full dilatation, the pH_s was determined (MBO = 7.27) and the perineum infiltrated (200 mg lidocaine) prior to episiotomy. Bearing-down efforts were readily accompanied by progressive fetal bradycardia. The delivery was achieved by vacuum extraction. The baby was depressed at 1 minute but readily recovered (APGAR scores 2—8). At birth, the pH_a is 7.13.

2.4 Biochemical state of the fetus at the end of the first stage of labor

Only one individual scalp blood pH (Tab. IV and V) was abnormal (A 20, Figs. 2—4). The mean pH values for primiparae and multiparae (Tab. VI) were 7.33 (± 0.02) and 7.34 (± 0.01), respectively.

One concludes that if there is no myometrial hypertonicity, the scalp blood pH is normal, which means that **the infusion of PGF2α has no influence on the acid-base status of the fetus during the first stage of labor.**

2.5 Biochemical state of the infant at birth

With two exceptions (A 20 and B 21), the individual pH values of umbilical-artery blood were normal (Tab. IV and V). The mean values of a number of components of the acid-base equilibrium are given in Tab. VI. Comparison with the values of the normal controls, i. e. "clinically normal cases" in which no oxytocic substances were administered, shows **no statistically significant differences except for the mean base excess in the umbilical-artery blood of the multiparous** group.

Tab. VI. Fetal biochemical status at birth.

		ΔXL_{f-m} [mg/100 ml plasma]	pH_a	BE_a [mEq/l]	SB_a [mEq/l]	$pCO_{2(a)}$ [mmHg]	$pO_{2(a)}$ [mmHg]
Primiparae	PGF2α	6.80±1.39 (27)	7.269±0.015 (30)	—8.88±0.51 (30)	17.61±0.33 (30)	48.3±2.0 (30)	16.4±0.8 (30)
	Controls	3.89±0.88 (48)	7.301±0.008 (55)	—7.52±0.35 (52)	18.37±0.25 (52)	43.5±2.3 (27)	19.1±1.3 (17)
	t-test (Student)	1.86	1.95	2.25	1.84	1.59	1.96
Multiparae	PGF2α	2.70±1.11 (22)	7.313±0.012 (24)	—5.55±0.48 (24)	19.97±0.35 (24)	43.9±1.7 (24)	19.3±1.2 (24)
	Controls	1.85±0.64 (86)	7.326±0.006 (93)	—5.92±0.26 (91)	19.51±0.19 (91)	43.1±1.2 (58)	19.0±0.7 (38)
	t-test (Student)	0.62	0.97	0.66	1.13	0.38	0.26

* Mean values ± SE. Between brackets the number of cases is given
a = blood from A. umbilicalis
ΔXL_{f-m} = fetal-maternal difference in excess lactate
BE and SB = base excess and standard bicarbonate

2.6 Clinical state of the infant at birth (Tab. IV and V)

Nine of the 1-minute APGAR scores are abnormal (< 7). At the 5-minute check all were normal except one (B 15), but the acid-base status of this infant was nevertheless within normal limits.

2.7 Postpartum morbidity and clinical condition of the mother and infant at discharge

The postpartum course of the mothers and newborns was uneventful. There was one instance (A 23) of early postpartum hemorrhage, easily checked with an intravenous infusion of oxytocin. All of the babies are being followed up both physically and mentally. The results of this investigation will be published separately.

3. Discussion

A systematic scheme of treatment was followed in the present study and the subgroups (primi- vs. multiparae) are comparable. **Parity proved not to have any dramatic influence on the effectiveness of the procedure.** The correlation coefficient between the BISHOP score and the duration of labor was —0.61 for the primiparae and —0.70 for the multiparae. In the latter group, one odd case (B 21) was excluded for statistical reasons. **The only dangerous side-effect** to be taken into consideration when using combined induction at term (especially in primiparae) is **overdosage of PGF2α, which can lead to uterine hypertonicity.** Indeed, in 2 out of 3 instances a rise of the basal tone above 12 mmHg was accompanied by a deceleration, albeit transient, of the FHR. If hypertonus occurs, the PG infusion should be stopped immediately and the fetus should be allowed to recuperate while still in utero. Immediate delivery by either route should be avoided if the hypertonus is alleviated. Only when uncontrollable and persistent hypertonus and bradycardia occur is emergency delivery indicated, although it will rarely "save" the fetus. If, however, the dose titration is carefully conducted under continuous monitoring, we consider that a limit need not be put on the dose of PGF2α applied, as is clearly shown by at least one of our cases (B 21). It should nonetheless be stated unequivocally that — compared to synthetic oxytocin infused intravenously — **PGF2α is a rather tricky drug, because it is much more difficult to titrate adequately,** i. e. toxic levels (hypertonus) are not much higher than effective ones (active labor) [7, 11]. Consequently, it is our contention that the use of PGF2α for the elective induction of term labor should be restricted to institutions

equipped for active and adequate electronic supervision.

One last point may be stressed. The reactivity pattern of the unborn during the second stage of labor, which is otherwise normal up to this point, cannot be foreseen [9]. Since cord blood examination and the clinical state of the infant at birth correlate better and virtually exclusively with the events that have taken place at the end of the first and during the second stage of labor, only scalp blood examination at full dilatation allows correct evaluation of the effect of PGF2α on the fetus during labor. Since the expulsive stage is the most hazardous period in the life of the unborn, the use of a monitoring device is mandatory to diagnose such abnormal FHR patterns as persistent bradycardia, which are deleterious if not fatal to the fetus.

4. Conclusions

Combined (amniotomy + titrated administration of PGF2α) elective induction of term labor is acceptable and harmless to the mother. The level of effectiveness of this procedure correlates with adequate drug titration. A **maximal dose level** (or total dose) **of PGF2α cannot be defined.** If overdosage of PGF2α is avoided, the hazards to the fetus and the neonate are not significantly increased by the use of this drug. Since we consider that to be adequate, titration of intravenous PGF2α should be continuously supervised, **facilities for electronic surveillance of the FHR** and proper recording of intra-amniotic pressure varations are **indispensable.**

Summary

Intravenous Prostaglandin F2α and amniotomy for the elective induction of labor at term

The present study has the dual purpose of investigating the **effect of prostaglandin F2α (PGF2α) on the fetus and the newborn by** relying on a procedure actually used in clinical obstetrics, i. e. amniotomy followed by the intravenous infusion of an oxytocic drug.

Material and methods

The selection criteria of the patients, which have been described previously [6], permitted us to eliminate any other factor that might influence the unborn.

73 candidates, inducible according to the BISHOP pelvic scoring system [1], underwent low amniotomy and were hooked to a fetal monitor. After 60 minutes of observation 18 women were judged to be in active labor (> 100 Montevideo Units) and were excluded from the study. This left us with a **total of 55 women** (30 primi- and 25 multiparae) **in whom intravenous infusion of PGF2α in saline was started** by pump at a dosage of 2,0 μg/min. The dose was increased at intervals of 15—60 minutes until "adequate" contractions were recorded, decreased if signs of uterine hyperstimulation were obtained or pathological fetal heart rate (FHR) patterns recorded (Tab. IV and V); in occasional cases the infusion was stopped and, eventually, prudently resumed.

The monitoring data were evaluated separately according to own standards for the first [10] and the second [9] stage, **the fetal status being assessed** in between, i. e. at full dilation, **by scalp blood pH.**

Delivery was spontaneous (n = 41) or assisted by vacuum extraction (n = 14). At birth, the infant were fully investigated clinically and biochemically, i. e. by determination of the acid-base and lactate-pyruvate equilibria [2, 5, 6].

Results

The **induction succeeded in all the cases** (Tab. I and II), carrying **little or no side-effects** and not disturbing the acid-base balance in the mother.

In three primiparae first stage labor was complicated by transient hypertonus with simultaneous FHR anomalies (Fig. 1—4) in two instances, one fetus (A 20) being acidotic and hypoxic at birth. A fourth primipara showed bouts of variable deceleration of the FHR in the first stage without influence on the child. Prolonged expulsion, i. e. more than 10 forceful contractions, occurred in 3 cases without untoward fetal effects.

Except for one case (A 20), scalp blood pH at the end of the first stage was normal. At the time of delivery (Tab. IV and V) two babies (A 20 and B 21) were acidotic. **The mean values of a number of components of the acid-base equilibrium (Tab. 6) did not show statistically significant differences from the controls** except for the base-excess in umbilical artery blood of the multiparae.

Nine APGAR scores were low (< 7) at one minute and one at 5 minutes. The postpartum and the newborn period were uncomplicated.

Discussion

The only dangerous side-effect to be taken into consideration, especially in primiparae, is **overdosage of PGF2α** which can lead to **uterine hypertonicity.** Indeed, in 2 out of 3 instances a rise of the basal tone above 12 mmHg was accompanied by a deceleration, albeit transient, of the FHR. If hypertonus occurs, the PG infusion should be stopped immediately.

Compared to oxytocin infused intravenously, **PGF2α is a rather tricky drug, because it is much more difficult to titrate adequately,** i. e. toxic levels (hypertonus) are not very remote from the effective ones [7, 11]. As a consequence the use of PGF2α for the induction of term labor should, for the time being, be restricted to institutions fully equipped for fetal monitoring.

Conclusion

Provided facilities are available for the continuous electronic surveillance of the fetus, elective induction of term labor with amniotomy and titrated intravenous administration of PGF2α is an acceptable procedure. **The main hazard to the fetus consists of hypoxia resulting from uterine hypertonus.**

Keywords: acid-base balance, excess lactate, fetal monitoring, induction of labor, prostaglandins.

Zusammenfassung

Intravenöse Anwendung des Prostaglandins F2α und Blasensprengung zur gezielten Weheneinleitung am Geburtstermin

Die vorliegende Studie verfolgt den Zweck, die **Wirkung des Prostaglandins F2α (PGF2α) auf den Feten und das Neugeborene** zu erforschen unter gleichzeitiger Anwendung einer Methode die tatsächlich in der klinischen Geburtshilfe angewendet wird, nämlich die Blasensprengung mit anschließender intravenöser Infusion eines Wehenmittels.

Material und Methode

Die schon früher von uns beschriebenen Ausfallkriterien [6] ermöglichten alle anderen, das ungeborene Kind möglicherweise beeinflussenden Faktoren auszuschließen.
Bei 73 Schwangeren, die nach dem Bishop Pelvic Scoring System [1] einleitungsbereit waren, wurde eine untere Amniotomie durchgeführt und ein Kardiotokograph angeschlossen. Nach 60 Minuten Beobachtungszeit wurde bei 18 Frauen festgestellt, daß die Geburt aktiv ingang gekommen war (über 100 Montevideo Einheiten). Diese wurden von der Studie ausgeschlossen. Bei den restlichen 50 Frauen (30 Erst- und 25 Mehrgebärende) wurde über eine Pumpe eine **intravenöse Infusion von PGF2α** in physiologischer Kochsalzlösung **mit einer Dosis von 2,0 μg/min** angelegt. Die Dosis wurde in Zeitabständen von 15—60 Minuten gesteigert bis adäquate Kontraktionen festgestellt wurden, und wieder herabgesetzt, sobald Zeichen einer uterinen Überstimulation oder pathologische fetale Herzfrequenzmuster festgestellt wurden (Tab. IV und V); gelegentlich wurde die Infusion auch völlig abgestellt und eventuell vorsichtig wieder aufgenommen.
Die Überwachungsdaten wurden getrennt für die Eröffnungsperiode [10] und die Austreibungsperiode [9] ausgewertet, entsprechend den jeweils gültigen Normwerten zwischen beiden Phasen, d. h. zum Zeitpunkt der vollen Eröffnung des Muttermundes wurde der Zustand des Feten durch eine Kopfschwartenblut pH-Messung untersucht.
Die Entbindung erfolgte spontan (n = 41) oder durch Vacuum-Extraktion (n = 14). Zum Zeitpunkt der Geburt wurden die Neugeborenen klinisch auch und biochemisch, d. h. durch Bestimmung des Säure-Base-Haushaltes und des Lactat-Pyruvat-Gleichgewichtes [2, 5, 6] untersucht.

Ergebnisse

Die Einleitungen hatten in allen Fällen (Tab. I und II) Erfolg, wobei **wenige oder gar keine Nebenwirkungen** auftraten und der Säure-Base-Haushalt der Mutter nicht gestört wurde.
Bei drei Erstgebärenden trat in der Eröffnungsperiode ein **vorübergehender Hypertonus auf** mit gleichzeitigem abnormem fetalem Herzfrequenzmuster in zwei Fällen, (Figs. 1—4) wobei ein Fet (A 20) zum Zeitpunkt der Geburt azidotisch und hypoxisch war. Bei einer vierten Erstgebärenden traten anfallsweise variable Tiefs der fetalen Herztöne in der ersten Geburtsphase auf ohne Einfluß auf den Zustand des Kindes. Eine verzögerte Austreibung, d. h. mehr als 10 kräftige Kontraktionen, trat in 3 Fällen auf, ohne daß dies den Feten beeinträchtigt hat.
Außer in einem Fall (A 20) war die Untersuchung des pH des Kopfschwartenblutes beim Feten am Ende der Eröffnungsperiode normal. Zum Zeitpunkt der Geburt (Tab. IV und V) waren zwei Neugeborene (A 20 und B 21) azidotisch. Die Mittelwerte der verschiedenen Meßdaten des Säure-Base-Haushaltes (Tab. IV) zeigten keine statistisch signifikante Unterschiede zur Kontrollgruppe mit Ausnahme des Basen-Exzeß im Nabelschnurarterienblut bei Mehrgebärenden.
Neun Apgar-Werte lagen niedrig (< 7) nach einer Minute und ein Wert nach 5 Minuten. Die Postpartalperiode und die Neugeborenenperiode waren ohne Komplikationen.

Diskussion

Die **einzige gefährliche Nebenwirkung** die in Betracht gezogen werden muß, **insbesondere bei Erstgebärenden,** ist die Überdosierung von PGF2α die zu einer **Dauerkontraktion** führen kann. Tatsächlich war in zwei von drei Fällen ein Anstieg des Basaltonus über 12 mmHg von einem wenn auch vorübergehenden Abfall der fetalen Herzfrequenz begleitet. Tritt ein übermäßiger Uterustonus auf, so sollte die PG-Infusion unverzüglich eingestellt werden. Verglichen mit Oxytocin ist das PGF2α bei intravenöser Anwendung eine ziemlich schwierig zu dosie-

rende Substanz, da die **adäquate Dosiseinstellung viel schwieriger** ist, d. h. die toxische Dosis (Dauerkontraktion) liegt nicht weit entfernt von der effektiven Dosis [7, 11]. Daraus ergibt sich, daß die **Anwendung des PGF2α** zur Einleitung der Wehen am Geburtstermin **gegenwärtig noch beschränkt** sein sollte **auf Abteilungen, die für die fortlaufende Überwachung des Feten voll ausgerüstet sind.**

Schlußfolgerung

Wenn die Möglichkeit einer fortlaufenden elektronischen Überwachung des Feten gegeben ist, so ist die gezielte Weheneinleitung am Termin durch Amniotomie und genau dosierte intravenöse Gabe von PGF2α eine brauchbare Methode. Die Hauptgefahr für den Feten besteht in der Hypoxie infolge eines erhöhten Uterustonus.

Schlüsselworte: fetale Überwachung, Laktat-Überschuß, Prostaglandine, Säure-Base-Haushalt, Weheneinleitung.

Résumé

Perfusion intraveineuse de Prostaglandine F2α et amniotomie pour l'induction du travail d'accouchement

Le présent travail a été entrepris dans le double but d' étudier les **effets de la prostaglandine F2α (PGF2α) sur le foetus et le nouveau-né,** d'après une procédure utilisée actuellement en pratique obstétricale: l'amniotomie suivie de la perfusion intraveineuse d'un ocytocique.

Matériel et Methode

Une sélection sévère, sur la base de critères décrits précédemment [6], a permis d'éliminer tout autre facteur qui pourrait influencer le foetus.

Septante-trois candidates, avec indices favorables d'après le système de Bishop [1], ont été soumises à une amniotomie et connectées à un moniteur foetal. Après 60 minutes d'observation 18 femmes furent jugées être en travail d'accouchement (> 100 unités-Montevideo) et exclues de l'étude. Dès lors il nous restait au total 55 **femmes** (30 primi- et 25 multipares) **qui furent soumises,** à l'aide d'une pompe à débit constant, **à une perfusion intraveineuse de PGF2α** dans du serum physiologique à la dose de 2,0 μg/min. La dose fut augmentée à intervalles de 15—60 minutes de façon à obtenir des contractions adéquates; elle fut diminuée ou même réduite à zéro à l'apparition de signes d'hyperstimulation utérine ou d'un tracé pathologique de l'enrégistrement de la fréquence cardiaqe foetale (FCF) (Tab. IV et V).

Les données en provenance du moniteur ont été évaluées d'après des critères personnels, séparément pour la période de dilation [10] et la période d'expulsion [9]. A dilatation complète, **l'état du foetus fut apprécié par la détermination du pH du sang capillaire.**

L'accouchement fut spontané (n = 41) ou assisté par extraction à la ventouse suédoise (n = 14). A la naissance l'enfant a fait l'objet d'un bilan clinique et biochimique, comportant l'indice d'Apgar et les équilibres acido-basique et lacticopyruvique [2, 5, 6].

Résultats

L'induction du travail d'accouchement a réussi dans tous les cas (Tab. I et II) sans occasioner de complications maternelles notables et sans modifier l'équilibre acidobasique de la parturiente.

Chez trois primipares la période de dilatation fut compliquée d'hypertonie utérine transitoire, associé dans deux cas d'anomalies simultanées de la FCF (Figs. 1—4), l'un de ces deux foetus (A 20) présentant de l'acidose et de l'hypoxie à la naissance. Une quatrième primipare a montré, également pendant la période de dilatation, des accès de décélération variable de la FCF, toutefois sans autre répercussion foetale. Une prolongation de la période d' expulsion, c. à. d. comportant plus de dix contractions vigoureuses, s'est rencontrée trois fois sans entrainer d' effets nocifs sur le foetus.

A l'exception d'un seul cas (A 20) le pH du sang foetal était normal à la fin de la période de dilatation. A la naissance (Tabs. IV et V) deux enfants (A 20 et B 21) souffraient d'acidose. Cependant, **les valeurs moyennes de plusieurs composants de l'équilibre acido-basique et lacticopyruvique ne différaient pas statistiquement des valeurs-témoins** à l'exception de l'excès de base dans le sang de l'artère ombilicale chez les multipares.

Neuf indices d'Apgar étaient bas (< 7) à une minute et un à 5 minutes. Le postpartum et la période néonatale furent sans particularités.

Discussion

Un seul **effect secondaire dangereux** est à prendre en considération, spécialement chez le primipare: le surdosage de la PGF2α, qui peut entrainer une **hypertonie utérine.** En effet, dans 2 des 3 cas, une augmentation du tonus de base au dessus de 12 mmHg s'accompagnat de décélération, bien que transitoire, de la FCF. Si l'hypertonie se produit, la perfusion de PFG2α doit être arrêtée immédiatement.

Comparée à l'ocytocine en perfusion intraveineuse, **la PGF2α est une substance délicate à manier, parce qu'il est de loin plus difficile de la titrer de façon adéquate:** la dose toxique (hypertonie) est de peu supérieure à la dose effective [7, 11]. Dès lors, l'emploi de la PGF2α pour l'induction du travail d'accouchement devrait être, pour le temps présent, restreinte aux institutions équipées d'un moniteur foetal.

Conclusions

A condition de disposer d'une instrumentation électronique qui permette la surveillance étroite du foetus, l'induction élective du travail d'accouchement à terme par amniotomie et administration intraveineuse titrée de PGF2α est une procédure acceptable. Le **risque principal pour le foetus est l'hypoxie suite à une hypertonie utérine.**

Mots-clés: équilibre acido-basique, excès de base, induction du travail, prostaglandins, surveillance du foetus.

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